

**A METHOD OF IDENTIFICATION OF INHIBITORS  
OF PDE1C AND METHODS OF TREATMENT OF DIABETES**

Abstract of the Disclosure

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The present invention provides a method of identifying novel agents that increase glucose dependent insulin secretion in pancreatic islet cells as well as methods of treating diabetes using the agents which have an inhibitory effect on the activity of pancreatic islet cell phosphodiesterases ("PDE") enzyme, namely PDE1C. The methods described herein are based upon the inventor's surprising discovery that inhibition of PDE1C increases glucose dependent insulin secretion. Specifically, the present invention provides for a method of identifying therapeutic agents that act to increase the release of insulin from pancreatic islet cells. The method of identification provided herein is used to determine the effects of isozyme specific phosphodiesterase inhibitors on insulin secretion from cultured pancreatic  $\beta$ -cells. Also provided are agents that have an inhibitory effect on the activity of PDE1C in pancreatic cells. Further provided is a method of treating diabetes comprising administering to a subject an amount of a PDE1C inhibitor effective to treat the type II diabetes.